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10/802,153	03/17/2004	Zhi-Jian Yu	AMOINC.001CP1	3939

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
01/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/802,153	YU ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-23* is/are pending in the application.

4a) Of the above claim(s) *18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 8/31/2007, in reply to the Office Action mailed 7/17/2007, is acknowledged and has been entered. The Supplemental Response, filed 11/05/2007 is also acknowledged and has been entered. Claims 1, 8, 14 and 17 have been amended. Claim 5 has been cancelled. Claims 1 – 4 and 6 – 23 are pending, of which claims 18 – 23 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1 – 4 and 6 – 17 are readable upon the elected invention and are examined herein on the merits for patentability.

Response to Arguments

Applicant's request, see page 5 of the Response, to hold in abeyance the provisional rejection of claims 1 – 17 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of Applications 10/392,375, 11/098,827 and 11/417,891, in view of Noecker, is acknowledged. The rejections are MAINTAINED for reasons of record.

Applicant's arguments, see page 5 of the Response, with respect to the rejection of claims 8, 14 and 17 under 35 U.S.C. 112, second paragraph, have been fully considered. The rejection has been WITHDRAWN as being overcome by amendment.

Applicant's arguments, see page 5 of the Response, with respect to the rejection of claims 1 – 6, 9, 10 and 12 – 16 under 35 U.S.C. 102(e) as being anticipated by Huth *et al.* (US 2003/0165545) have been fully considered. The rejection has been WITHDRAWN as being overcome by amendment.

Applicant's arguments, see pages 5 – 6 of the Response, with respect to the rejection of claims 1 – 3, 6 – 8, 10, 11, 15, 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over Goto (*Ophthalmology*, 2002, 109, p. 2030-2035) in view of Noecker (*Adv. Ther.*, 2001, 18, p. 205 - 215) have been fully considered but are not persuasive. The rejection is MAINTAINED for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 – 3, 6 – 8, 10, 11, 15, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goto (*Ophthalmology*, 2002, 109, p. 2030-2035) in view of Noecker (*Adv. Ther.*, 2001, 18, p. 205 - 215), for reasons set forth in the Office Action mailed 7/17/2007.

Applicant argues on pages 5 – 6 of the Response that the Goto reference was published in November 2002, which was less than one year prior to the effective filing date of the present application, March 18, 2003. Applicant provided the Declaration of inventors Yu, Huth, Crawford and Cook as well as Exhibit A in order to antedate the

Goto reference, and argues that the Goto reference is not prior art to the instant invention.

However, as evidenced by the attached abstract, the Goto reference was available online October 14, 2002. As such, the declaration that the invention was reduced to practice prior to November 2002, in combination with Exhibit A, is not sufficient to antedate the reference. No further arguments were presented regarding the grounds for rejection, thus the rejection is maintained.

New Grounds for Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 4, 6, 7, 9 –13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al* (US 6,458,373) in view of Noecker (*Adv. Ther.*, 2001, 18, p. 205 – 215).

Lambert discloses an emulsion of α-tocopherol, stabilized by biocompatible surfactants, as a vehicle or carrier for therapeutic drugs, which is substantially ethanol free and which can be administered to animals or humans various routes. Also included in the emulsion is PEGylated vitamin E. PEGylated α-tocopherol includes polyethylene glycol subunits attached by a succinic acid diester at the ring hydroxyl of vitamin E and serves as a primary surfactant, stabilizer and a secondary solvent in emulsions of α-tocopherol (abstract). The invention is directed to pharmaceutical compositions in the form of emulsions, micellar solutions or self-emulsifying drug delivery systems which are substantially free of ethanol (column 9, lines 1 – 5). A variety of therapeutic compounds may be incorporated into the compositions (see column 8). The composition containing tocopherol as a carrier for therapeutic drugs may be delivered via a variety of routes, including intraocular (column 9, line 20). PEGylated vitamin E (TPGS) is used as a primary surfactant in emulsions of vitamin E (i.e. a polar oil). PEGylated vitamin E is utilized as a primary surfactant, a stabilizer and also as a supplementary solvent in emulsions of vitamin E. Polyethylene glycol (PEG) is also useful as a secondary solvent in the emulsions of this invention (column 9, lines 60+). The emulsions may further include additional surfactants such as ascorbyl-6-palmitate, stearlyamide, or non-ioninc synthetic surfactants (column 10, lines 5 – 12). The emulsions include an aqueous medium, including antimicrobial preservatives, etc. The particle size is 10 – 500 nm (column 10, lines 13 – 30).

Lambert does not teach a chlorite preservative.

Noecker teaches that preservatives are an important component of ophthalmic preparations, providing antimicrobial activity in the bottle and preventing decomposition of active drug. Stabilized oxychloro complex (SOC) causes the least amount of damage to corneal epithelial cells compared to other preservatives. Physicians should consider treatment with preparations containing low-risk preservatives, such as SOC, especially in patients receiving multiple ophthalmic medications (abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to include a preservative such as SOC in the compositions of Lambert, when intended for intraocular applications, because Noecker teaches that such preservatives provide the advantage of providing antimicrobial activity in the bottle of ophthalmic formulations. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Noecker teaches that SOC has a low toxicity compared to other preservatives.

Claims 1 –7 and 9 – 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huth *et al.* (US 2003/0165545) in view of Lambert *et al* (US 6,458,373).

Huth discloses self-emulsifying compositions for ophthalmic use, such as the care of contact lenses (paragraph 0007 – 0008). The oil-in-water emulsions comprise an oily component, for example, and without limitation, mineral oil, castor oil; an aqueous component, which includes water; and a surfactant component which includes at least three emulsifiers or surfactants (paragraph 0012, 0045). An example of a

surfactant may be 10-mole ethylene oxide ether of stearyl alcohol (paragraph 0051 or vitamin E TPGS (paragraph 0137). The compositions may include a chlorite preservative (paragraph 0133), and may include a disinfectant such as Polyquaternium (paragraph 0126) and a therapeutic component (paragraph 0097). Globules of the emulsion must pass through a 0.22 micron filter (paragraph 0142).

Huth teaches that the emulsions include three surfactants, rather than one or two surfactants, as claimed.

However, the formation of a self-emulsifying oil-in-water emulsion using TPGS as a single surfactant, rather than one of three surfactants, is known in the art as shown by Lambert.

Lambert discloses self-emulsifying emulsions comprising α-tocopherol and stabilized by a TPGS surfactant as a vehicle or carrier for therapeutic drug, as set forth above.

It would have been obvious to one or ordinary skill in the art at the time of the instant invention to modify the teachings of Huth to include one or two, rather than three surfactants. The preparation of various pharmaceutical compositions having various amounts of active agent is within the level of skill of one having ordinary skill in the art at the time of the invention. One would have been motivated to do so as a matter of optimizing the formulations and Huth, and would have had a reasonable expectation of success in doing so because Lambert teaches self-emulsifying emulsions having TPGS as a single surfactant, but which may optionally include additional surfactant components. With these things in mind a skilled artisan would have been motivated to

combine the teachings of Huth with those of Lambert in order to provide a stable emulsion formulation capable of intra-ocular administration.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER